

WHAT IS CLAIMED IS:

1. An assay comprising:  
culturing microglial cells with a test compound; and  
determining the effect of the compound on microglial activation;  
wherein activation of said microglial cells is determined by a measurable change in a  
particular cellular activity.
2. The assay of claim 1, wherein the measurable change in cellular activity is  
increased cytokine expression.
3. The assay of claim 1, wherein the test compound alters a prostaglandin E<sub>2</sub>-  
mediated pathway.
4. The assay of claim 1, wherein the effect of the compound is determined by  
comparing the effect with a control culture in absence of the compound.
5. The assay of claim 1, wherein the effect of the compound is determined by  
comparing the effect with a standardized profile of the particular cellular activity.
6. The assay of claim 2, wherein the cytokine is selected from the group consisting  
of TNF- $\alpha$ , IL-1 $\alpha$  and IL-6.
7. An assay to identify compounds which alter, halt or prevent progression of an  
amyloid-associated disorder, comprising the steps of:  
obtaining a sample comprising microglial cells which express cytokines at a known level;  
contacting the cells with an A $\beta$  peptide;  
contacting the cells with a test compound; and

5 determining the synergistic effects of the A $\beta$  peptide with the expressed cytokines;  
wherein the synergistic effect of the A $\beta$  peptide and the cytokine is indicative of the  
therapeutic ability of the compound to halt progression of the disorder.

10 8. The assay of claim 7, wherein the disorder is AD, and wherein the cytokine is IL-  
1 $\alpha$ .

9. The assay of claim 7, wherein the compound affects cytokine levels through a  
prostaglandin-mediated pathway.

15 10. The assay of claim 9, wherein the compound affects an EP4 isoform of the  
prostaglandin E<sub>2</sub> receptor, and wherein a reduced synergistic effect is indicative of the function of  
that isoform in the amyloid-associated disorder.

20 11. The assay of claim 7, wherein the assay is conducted using a plurality of different  
samples, and wherein the assay is conducted using different doses of the test compound.

25 12. A compound that inhibits A $\beta$ :PGE<sub>2</sub> mediated microglia activation, wherein said  
compound is identified by a method comprising the steps:  
culturing microglial cells with a compound; and  
determining the effect of the compound on microglial activation;  
— wherein the cultured microglia exhibit decreased cytokine expression upon exposure to  
the compound.

30 13. The compound of claim 12, wherein the compound is a prostaglandin E<sub>2</sub>  
antagonist.

5           14.     The compound of claim 13, wherein the compound alters activity through the prostaglandin E<sub>2</sub> EP4 isoform.

          15.     A method for reducing the level of  $\beta$ -amyloid plaque in the brain tissue of a mammalian host, said method comprising:

10           administering to said mammalian host a compound in an amount effective to reduce microglial activation,

          wherein the lowered microglial activation results in reduced cytokine secretion in brain tissue.

15           16.     The method of claim 15, wherein the administered compound is a compound of claim 12.

          17.     The method of claim 16, wherein the microglial activation is reduced 30 to 80%, and wherein cytokine secretion levels are reduced 20 to 80%.

20           18.     A method for preventing the formation of amyloid plaques in the brain of a mammal at risk for an amyloid-associated disorder, said method comprising:

          administering to said mammal a compound in an amount effective to reduce microglial activation;

25           wherein the compound results in reduced cytokine secretion from microglial cells.

          19.     The method of claim 18, wherein the compound administered is a compound of claim 12.

30           20.     The method of claim 18, wherein the mammal is at risk for AD is a human and the compound decreases cytokine production via a prostaglandin E<sub>2</sub>-mediated pathway.

- 5           21.    A method for treating a mammal with an amyloid-associated disorder, said  
method comprising:  
          administering to said patient a compound in an amount effective to inhibit a  
prostaglandin E2 receptor;  
          wherein the activity of compound results in a decrease in plaque formation in brain tissue.

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